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Research Article



Predicting Factors of Pain Duration in Patients with Chronic Pain: A Large Population-based Study

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Abstract

Background: Chronic pain is the third main problem of global health and the most common cause of long-term disabilities. The duration that patients suffer from chronic pain is directly proportional to the extent of the suffering and to the amount of health care resources allocated to this problem. There is no research that has studied the risk factors associated with the long pain duration in chronic pain patients.

Methods: We investigated the potential risk factors associated with long pain duration in a population with diverse pain conditions in a cross-sectional study. We used a questionnaire that included a number of potential risk factors including sex, age, marital status, household condition, number of children, employment, education, body mass index (BMI), pain intensity, and the level of anxiety/depression. The data were analyzed by univariable and multivariable linear regression models.

Results: We recruited 780 patients. The analyses showed that age and abnormal BMI had a positive correlation with pain duration. **Conclusions:** The risk factors that might be associated with longer pain duration include older age and abnormal BMI.

Keywords: Pain, Duration, Obesity, BMI, Sex, Gender, Age, Treatment, Management, Chronic

1. Background

Chronic pain is the third main problem of global health and the most common cause of long-term disabilities. The total number of working days lost due to chronic pain is about 50 million days a year in the United States (1). Chronic pain is a complicated health problem that is associated with significant psychological co-morbidities, including somatization, depression, and anxiety. It affects sleeping and eating habits, reduces physical and professional activities, limits personal income, and impairs interpersonal relationships (2, 3).

The duration that patients suffer from chronic pain has variable lengths. A certain chronic pain condition lasts longer or even persists forever in some patients while the same condition subsides sooner in other patients. Pain duration (PD) is directly proportional to the extent of the suffering and to the amount of health care resources that allocated to this problem. Long PD may have many reasons including the chronic nature of the underlying condition, delayed referring to pain clinics, and inadequate

pain treatment (IPT). Our information is very limited concerning the risk factors associated with long PD. Some investigations have studied the socioeconomic parameters that may have an impact on chronic pain (4-8). However, to the best of our knowledge, there is no research that has studied the risk factors associated with long PD in chronic pain patients. Most studies have only reported the average duration of pain in these patients whereas we tried to determine the risk factors associated with PD. Our comprehensive knowledge of associated risk factors for longer PD in chronic pain patients can ultimately improve the treatment outcome and save a lot of health care resources.

2. Methods

In this cross-sectional study, we investigated the potential risk factors associated with long PD in a population with diverse underlying pain conditions who had referred to our tertiary pain clinic before we commenced our specialized pain treatments. This study was approved by

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the Ethics Committee of our university hospital. Informed consent was obtained from all patients.

The inclusion criteria were (a) patients with chronic pain, defined as PD of more than three months. Chronic pain conditions included: CRPS, fibromyalgia, phantom/stump pain, chronic persistent post-surgical pain, facetogenic pain, sacroiliac joint dysfunction, different kinds of poly/mono-neuropathies and neuralgias, migraine, atypical facial pain, trigeminal neuralgia, cluster-type headaches, piriformis syndrome, cervical/lumbosacral radicular pain, etc., (b) having adequate information or records of the previous pain management, (c) willingness to participate in the study, (d) having the mental capacity to fill in the questionnaire or cooperate with the interviewer, and (e) lack of any previous specialized chronic pain treatments including consuming tricyclic antidepressants, antiepileptics, SNRIs, SSRIs, or any specialized pain injection/block/denervation techniques. The exclusion criteria were (a) lack of chronic pain and (b) unwillingness to participate in the study.

We designed a self-report questionnaire that included a number of questions on the following potential risk factors (independent variables): sex, age, marital status, household condition, number of children, employment, education, body mass index (BMI), pain intensity (PI), and the level of anxiety/depression. Pain duration was also asked and recorded as the dependent variable. If the patient was unable to fill in the questionnaire, a trained staff was available to help him/her answer the questions.

Pain intensity was evaluated by the validated Persian version of the brief pain inventory (BPI) (9). The BPI is a multidimensional tool that contains a body diagram. The BPI has four numeric rating scales (NRS) to measure pain intensity at its least, worst, average, and current severity. Pain relief and interference with function, enjoyment, and mood can also be evaluated by BPI. Patients expressed their PI by an 11-point NRS with four questions: minimal PI, maximal PI, right-now PI (PI at the time of the interview), and overall PI (PI that the patient had suffered from during the last week). The mean PI was defined as the mean of the maximal, right-now, and overall pain intensities. Eventually, the mean PI was calculated and recorded for each patient.

Patients' education was classified into (a) illiterate, (b) below high school: having some education but less than high school diploma, (c) high school diploma: graduated from high school, (d) BS (Bachelor of Science) or lower: having some university education, (e) MS (Master of Science) or Ph.D.: having post-graduate training.

Marital status was classified into two groups: single (not being in any kind of relationship) and married (married or being in any type of relationship). The household condition was referred to as the number of people who

were living in a residential unit. We classified it into two groups: (a) alone (living alone) and (b) accompanied with others (living with someone else, whether a family member or a roommate). Patients were also classified into two groups based on their BMI: (a) normal BMI: 18.5 to 24.9 kg/m² and (b) abnormal BMI.

We evaluated the patients' level of anxiety and depression with the validated hospital anxiety and depression scale (HADS). This scale has 14 items. Each item is scored from 0 to 3. Therefore, patients could get a score from 0 to 42

2.1. Statistics

Data analysis was performed with SPSS 18. According to Elliott et al. (10), with a 10% reduction in the sample size and with a d = 0.04 and alpha = 0.05, the sample size was calculated about 660 patients. Data were expressed as frequency, percentage, and measures of central tendency such as mean, and measures of dispersion such as standard deviation. The distribution of data was evaluated using the Kolmogorov-Smirnov test. The correlation of continuous variables was evaluated by Pearson's correlation or Spearman's rho correlation test. The mean values of continuous variables in two categorical variables were done by 't' or Mann-Whitney test. A linear regression model was used to adjust for the independent variables. In the linear regression model, PD was the dependent variable while age, sex, job, education, BMI, PI, number of children, and household condition were the independent variables. We entered the mean PI, right-now PI, or minimal PI instead of maximal PI in other models. The p values of less than 0.05 were considered significant.

3. Results

We recruited 780 patients in this study. Their characteristics and descriptive data are shown in Table 1. The average PD was 60.52 months.

Tables 2 and 3 demonstrate the univariable analysis. We primarily evaluated the correlation between different potential risk factors and the outcome (dependent variable, PD). In the second step, the linear regression model (Table 4) was used to adjust for the independent variables. Table 2 shows that PD had a positive correlation with age, mean PI, and minimal and right-now PI in univariable analysis. Table 3 demonstrates that PD was significantly longer in females than in males (P = 0.008). Although PD was longer in unemployed patients and in people who were living alone, this difference was not significant.

In the linear regression models, PD was the dependent variable, while age, sex, employment, education, BMI, household condition, and different measures of PI were

Table 1. Patient Characteristics and Descriptive Data on Investigated Variables (N =

| Variable Mean \pm SD or Percentage | | |
|--------------------------------------|-------------------|--|
| Age, y | 49 ± 15.26 | |
| ≤30 | 12.0 | |
| 31 - 45 | 30.1 | |
| 46 - 65 | 41.2 | |
| > 65 | 16.7 | |
| Sex | | |
| Male | 43.6 | |
| Female | 56.4 | |
| Employment | | |
| Employed | 39.5 | |
| Unemployed | 60.5 | |
| Education | | |
| Illiterate | 14.2 | |
| Below high school | 38.7 | |
| High school diploma | 24.1 | |
| BS or lower | 18.4 | |
| MS or Ph.D. | 4.6 | |
| Marital status | | |
| Single | 19.6 | |
| Married | 80.4 | |
| Household conditions | | |
| Alone | 5.6 | |
| Accompanied with others ^a | 94.4 | |
| Number of children | 3.04 ± 2.09 | |
| BMI, kg/m ² | 25.7 ± 4.95 | |
| Normal (18.5 to 24.9) | 46.3 | |
| Abnormal | 53.7 | |
| Pain intensity (NRS) | | |
| Minimal | 2.90 ± 2.35 | |
| Maximal | 8.39 ± 1.94 | |
| Right-now | 5.22 ± 2.86 | |
| Overall | 6.76 ± 1.58 | |
| 'Mean Pain Intensity' b | 6.75 ± 1.78 | |
| HADS | 17.86 \pm 8.59 | |
| Pain duration, mo | 60.52 ± 88.99 | |

Abbreviations: BMI, body mass index; BS, bachelor of science; HADS, hospital anxiety and depression scale (0 - 42); MS, master of science; NRS, 11-point numeric rating scale.

Table 2. Correlation Between Pain Duration (Dependent Factor) and Independent Variables of Age, Education, and Different Pain Intensities

| Variables | Correlation Coefficient ^a | P Value |
|--------------------------|--------------------------------------|---------|
| Age | 0.135 ^b | 0.001 |
| Education | 0.032 ^b | 0.459 |
| 'Mean Pain intensity' | 0.102 ^c | 0.040 |
| Minimal pain intensity | 0.100 ^c | 0.035 |
| Right-now pain intensity | 0.120 ^c | 0.015 |
| Maximal pain intensity | 0.073 ^c | 0.120 |
| Overall pain intensity | 0.023 ^c | 0.619 |

 $^{^{\}mathrm{a}}1$ is a totally positive linear correlation, 0 is no linear correlation, and -1 is a totally negative linear correlation ^bPearson's correlation

Table 3. Comparison of Pain Duration Between the Groups of Sex, Employments, and Household Condition

| Variable | Mean Pain Duration, mo | Standard Deviation | PValue |
|---------------------------------|---------------------------|-----------------------|----------------------|
| Sex | | | 0.008 ^{a,b} |
| Male | 49.6 | 76.2 | |
| Female | 68.4 | 96.4 | |
| Employment | | | 0.528 ^b |
| Employed | 57.4 | 91.7 | |
| Unem- ployed | 62.3 | 87.0 | |
| Household condition | | | 0.114 ^c |
| Accompa- nied with others | 57.2 | 81.7 | |
| Alone | 98 | 137.9 | |

 $^{^{}a}$ Values show a significant correlation with pain duration (P value < 0.05).

the independent variables (Table 4). Age and abnormal BMI had a consistent positive correlation with PD in different models. Some other models were also tested. The results were similar when entering other measures of PI. Other independent variables did not show any significant relationship.

4. Discussion

This study demonstrated that older people and patients with abnormal BMI had longer PD among chronic pain patients. Therefore, age and abnormal BMI were independent risk factors of long PD. Female gender and higher mean PI were associated with longer PD in univariable

^aLiving with someone else in a residential unit.

^b'Mean Pain Intensity': the mean of the maximal, right-now, and overall pain intensities.

^cSpearman's rho correlation

^bt test

^cMann-Whitney test

Table 4. Linear Regression Analysis Between Pain Duration (Dependent Factor) and Independent Variables of Age, Sex, Employment, Education, BMI, Household Condition, and Maximal PI

| | Coefficients ^a | | | | |
|------------------------|-----------------------------|------------|---------------------------|--------|--------------------|
| Model | Unstandardized Coefficients | | Standardized Coefficients | t | P |
| | В | Std. Error | Beta | · | r |
| 1 | | | | | |
| (Constant) | -158.449 | 62.193 | | -2.548 | 0.012 |
| Age | 1.166 | 0.447 | 0.182 | 2.611 | 0.010 ^b |
| Sex | 14.071 | 14.189 | 0.075 | 0.992 | 0.322 |
| Employment | -2.067 | 14.347 | -0.011 | -0.144 | 0.886 |
| Education | 8.146 | 6.366 | 0.091 | 1.280 | 0.202 |
| BMI, kg/m ² | 2.978 | 1.281 | 0.160 | 2.325 | 0.021 ^b |
| Household condition | 30.892 | 28.197 | 0.072 | 1.096 | 0.274 |
| PI-maximal | 2.452 | 3.124 | 0.052 | 0.785 | 0.433 |

Abbreviations: BMI, body mass index: PI, pain intensity

analysis, which was not confirmed in multivariable linear regression models. Long PD in patients suffering from chronic pain can have many reasons including the chronic nature of the underlying condition, delayed seeking for medical care by the patients, delayed referral of the patients to pain clinics by health care providers, and Inadequate Pain Treatment (IPT).

Inadequate pain treatment can be an important reason for longer PD. When patients are not satisfied with their pain management or their pain is not adequately relieved, PD will be longer. Inadequate pain treatment is very common in chronic pain patients (11-13). Several factors have been proposed to contribute to IPT including age, gender, social status, and pain intensity (14-18). Our findings are comparable with these results. We observed that older patients, females, and patients with higher mean PI had longer PD, which could be attributed to more common IPT in this population. Older patients are also more prone to side effects of medications and they have a more fragile health condition. Therefore, some physicians are very cautious in the treatment of the geriatric population and they administer analgesics with low doses. Ultimately, it may lead to pain undertreatment of older patients.

There are many reports that IPT is more common in women (11, 19, 20), which are compatible with our results. Previous studies have indicated that race, ethnicity, gender, and socioeconomic factors would affect the people's health status and the use of medical care services (4-6). The importance of these factors in chronic pain has also been explained in several studies (4, 21, 22). Socioeconomic factors can modify individual pain experience (4-6, 10, 21-26). Women have a lower quality of pain management in dif-

ferent societies. In other words, IPT is more common in women (4, 19, 22, 27). There are some mechanisms that can explain this difference, including a different pain sensitivity or a different response to analgesics between the two genders (28-30) and a gender bias in the physician's prescription of potent analgesics (31). Consequently, IPT is more common in women and it may lead to longer PD.

We demonstrated that abnormal BMI is associated with longer PD. Prior studies have shown that obese patients reported higher pain intensities (32-35). Obesity is usually associated with a number of health issues including fatty liver, hypertension, insulin resistance, diabetes, depression, obstructive sleep apnea, and respiratory compromise (34, 36-38). It limits physicians to administer potent analgesics to these patients with adequate doses. Moreover, the volume of distribution and the rate of metabolism/elimination of analgesics are higher in obese patients due to the altered enzymatic activity by fatty liver-, which can decrease the efficacy of prescribed drugs (39, 40). Therefore, these patients are prone to pain undertreatment. On the other hand, physicians may be concerned to administer potent analgesics with adequate doses to underweight people because they may be easily overmedicated with usual doses due to their low body mass. Thus, that is why patients with abnormal BMI are usually prone to receive undertreatment; as a result, IPT would be more prevalent in this population, which can eventually lead to longer PD.

Our study was similar in gender distribution to the study by Rustoen et al. aiming to determine the prevalence and characteristics of chronic pain in the general Norwegian population. In both studies, chronic pain was more

^aDependent variable: pain duration (months). Negative and positive beta correlations represent inverse and straight relationships.

^bValues show a significant correlation with pain duration (P value < 0.05).

prevalent in females. These studies were also similar in the age distribution of patients. Meanwhile, the percentage of illiterate patients was higher in our study than in the Rustoen et al.'s report. It is expected that literate people would be more populated in countries with high annual income. The percentage of people who lived alone was higher in their study. Employed patients were more common in their study. Their sample was chosen from the general population while our patients were chronic pain patients referred to our public care service. It is reasonable that unemployment would be more common in disabled patients suffering from chronic pain with a lower annual income, which encouraged them to use public services rather than expensive private medical services. Unlike our study, Rustoen et al. (27) did not evaluate the relationship between different variables and PD.

Saastamoinen et al. investigated the relationship between socioeconomic variables and the prevalence of acute, chronic, and disabling chronic pain among employees. A questionnaire survey was conducted in 2000 - 2002 among employees aged 40, 45, 50, 55, and 60 (N = 8,970; response rate = 67%). Sociodemographic and socioeconomic factors and measures of current pain, PD, and pain-related disability were assessed. They demonstrated that patients with older age, lower education, and lower occupational class appeared to have a higher risk of chronic pain, especially disabling chronic pain. The results of this study are in line with our study that showed patients with older age appeared to be at excess risk of chronic pain. Also, the prevalence of chronic or disabling chronic pain was higher in females in both studies (41, 42).

Larsson et al. demonstrated a correlation between old age and persistent pain, which is similar to our study (42). However, their report showed that PD was more correlated with older females than senior men.

4.1. Limitations

Our sample was selected from the public sector; therefore, our patients were not a perfect representative of all chronic pain patients in society, especially those who used the private sector. Our patients had diverse underlying pain conditions; therefore, our results would have been more accurate if we had recruited all patients from a single chronic pain condition. Furthermore, the majority of the data were collected by a self-report questionnaire. In addition, illiterate patients or people with low levels of education usually have difficulty when they are asked to fill in the forms. Moreover, it is always possible that the investigators could not consider all possible confounding factors in their study or they could not think over all the possible logistic regression models.

4.2. Conclusion

The risk factors that might be associated with longer PD are older age and abnormal BMI.

Footnotes

Authors' Contribution: The idea of this research was developed by Hossein Majedi. Then, the idea and proposal were written and developed by all the authors. Hossein Majedi and Maryam Majedi designed the questionnaire. Hossein Majedi interviewed the patients. The data collection was accomplished by Hossein Majedi and Maryam Majedi. Data entry was done by Maryam Majedi and Mohammadreza Hoseini Amini. All authors participated in the manuscript preparation. Eventually, the manuscript was reviewed and edited by Hossein Majedi and Fardin Yousefshahi.

Conflict of Interests: There was no conflict of interests in this study.

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References

- Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain conditions in the US workforce. *JAMA*. 2003;290(18):2443-54. doi: 10.1001/jama.290.18.2443. [PubMed: 14612481].
- 2. Brookoff D. Chronic pain: 1. A new disease? *Hosp Pract* (1995). 2000;**35**(7):45–52. 59. doi: 10.1080/21548331.2000.11444031. [PubMed: 10916504]
- 3. Vo P, Marx S, Penles L. (374) Health-related quality of life (HRQoL) among patients experiencing acute and chronic pain: Results from a survey of 606 pain patients in the United States. *J Pain*. 2008;**9**(4):69. doi: 10.1016/j.jpain.2008.01.298.
- Green CR, Anderson KO, Baker TA, Campbell LC, Decker S, Fillingim RB, et al. The unequal burden of pain: confronting racial and ethnic disparities in pain. *Pain Med.* 2003;4(3):277-94. doi: 10.1046/j.1526-4637.2003.03034.x. [PubMed: 12974827].
- Swift EK. Guidance for the national healthcare disparities report. National Academies Press; 2002.
- Schneider EC, Zaslavsky AM, Epstein AM. Racial disparities in the quality of care for enrollees in medicare managed care. *JAMA*. 2002;287(10):1288-94. doi: 10.1001/jama.287.10.1288. [PubMed: 11886320].
- Pak DJ, Yong RJ, Kaye AD, Urman RD. Chronification of pain: Mechanisms, current understanding, and clinical implications. *Curr Pain Headache Rep.* 2018;22(2):9. doi: 10.1007/s11916-018-0666-8. [PubMed: 29404791].
- 8. Fletcher D, Stamer UM, Pogatzki-Zahn E, Zaslansky R, Tanase NV, Perruchoud C, et al. Chronic postsurgical pain in Europe: An observational study. *Eur J Anaesthesiol*. 2015;**32**(10):725-34. doi: 10.1097/EJA.00000000000000319. [PubMed: 26241763].
- Majedi H, Dehghani SS, Soleyman-Jahi S, Emami Meibodi SA, Mireskandari SM, Hajiaghababaei M, et al. Validation of the Persian version of the brief pain inventory (BPI-P) in chronic

- pain patients. J Pain Symptom Manage. 2017;**54**(1):132-138 e2. doi: 10.1016/j.jpainsymman.2017.02.017. [PubMed: 28479416].
- Elliott AM, Smith BH, Penny KI, Smith WC, Chambers WA. The epidemiology of chronic pain in the community. *Lancet*. 1999;354(9186):1248–52. doi: 10.1016/s0140-6736(99)03057-3. [PubMed: 10520633].
- Cleeland CS, Gonin R, Hatfield AK, Edmonson JH, Blum RH, Stewart JA, et al. Pain and its treatment in outpatients with metastatic cancer. N Engl J Med. 1994;330(9):592–6. doi: 10.1056/NEJM199403033300902. [PubMed: 7508092].
- Frich LM, Borgbjerg FM. Pain and pain treatment in AIDS patients: A longitudinal study. J Pain Symptom Manage. 2000;19(5):339–47. doi: 10.1016/s0885-3924(00)00140-8. [PubMed: 10869874].
- Gatti A, Sabato AF, Carucci A, Bertini L, Mammucari M, Occhioni R. Adequacy assessment of oxycodone/paracetamol (acetaminophen) in multimodal chronic pain: A prospective observational study. Clin Drug Investig. 2009;29 Suppl 1:31-40. doi: 10.2165/0044011-200929001-00005. [PubMed: 19445553].
- Becker N, Bondegaard Thomsen A, Olsen AK, Sjogren P, Bech P, Eriksen J. Pain epidemiology and health related quality of life in chronic nonmalignant pain patients referred to a Danish multidisciplinary pain center. *Pain*. 1997;73(3):393–400. doi: 10.1016/s0304-3959(97)00126-7. [PubMed: 9469530].
- Green CR, Baker TA, Ndao-Brumblay SK. Patient attitudes regarding healthcare utilization and referral: A descriptive comparison in African- and Caucasian Americans with chronic pain. *J Natl Med Assoc.* 2004;96(1):31–42. [PubMed: 14746352]. [PubMed Central: PMC2594747].
- Green CR, Tait RC, Gallagher RM. The unequal burden of pain: Disparities and differences. *Pain Med.* 2005;6(1):1-2. doi: 10.1111/j.1526-4637.2005.05017.x.
- Guck TP, Meilman PW, Skultety FM, Dowd ET. Prediction of long-term outcome of multidisciplinary pain treatment. Arch Phys Med Rehabil. 1986;67(5):293-6. [PubMed: 3707313].
- Weir R, Browne G, Tunks E, Gafni A, Roberts J. Gender differences in psychosocial adjustment to chronic pain and expenditures for health care services used. Clin J Pain. 1996;12(4):277-90. doi: 10.1097/00002508-199612000-00007. [PubMed: 8969873].
- Green CR, Hart-Johnson T. The adequacy of chronic pain management prior to presenting at a tertiary care pain center: The role of patient socio-demographic characteristics. *J Pain*. 2010;11(8):746–54. doi: 10.1016/j.jpain.2009.11.003. [PubMed: 20399710].
- McNeill JA, Sherwood GD, Starck PL. The hidden error of mismanaged pain: A systems approach. J Pain Symptom Manage. 2004;28(1):47–58. doi: 10.1016/j.jpainsymman.2003.11.005. [PubMed: 15223084].
- Green CR, Baker TA, Smith EM, Sato Y. The effect of race in older adults presenting for chronic pain management: A comparative study of black and white Americans. J Pain. 2003;4(2):82-90. doi: 10.1054/jpai.2003.8. [PubMed: 14622719].
- Green CR, Baker TA, Sato Y, Washington TL, Smith EM. Race and chronic pain: A comparative study of young black and white Americans presenting for management. *J Pain*. 2003;4(4):176–83. doi: 10.1016/s1526-5900(02)65013-8. [PubMed: 14622701].
- Gibson SJ, Helme RD. Cognitive factors and the experience of pain and suffering in older persons. *Pain*. 2000;85(3):375–83. doi: 10.1016/s0304-3959(99)00284-5. [PubMed: 10781910].
- Aggarwal VR, Macfarlane TV, Macfarlane GJ. Why is pain more common amongst people living in areas of low socio-economic status? A population-based cross-sectional study. Br Dent J. 2003;194(7):383-7. discussion 380. doi: 10.1038/sj.bdj.4810004. [PubMed: 12821918].
- Arfken CL, Lichtenberg PA, Tancer ME. Cognitive impairment and depression predict mortality in medically ill older adults. *J Gerontol A Biol Sci Med Sci*. 1999;54(3):M152-6. doi: 10.1093/gerona/54.3.m152. [PubMed: 10191844].
- 26. Green CR, Ndao-Brumblay SK, Nagrant AM, Baker TA, Rothman E.

- Race, age, and gender influences among clusters of African American and white patients with chronic pain. *J Pain*. 2004;**5**(3):171–82. doi: 10.1016/j.jpain.2004.02.227. [PubMed: 15106130].
- Rustoen T, Wahl AK, Hanestad BR, Lerdal A, Paul S, Miaskowski C. Prevalence and characteristics of chronic pain in the general Norwegian population. Eur J Pain. 2004;8(6):555-65. doi: 10.1016/j.ejpain.2004.02.002. [PubMed: 15531224].
- Fillingim RB. Sex differences in analgesic responses: Evidence from experimental pain models. Eur J Anaesthesiol Suppl. 2002;26:16–24. doi: 10.1097/00003643-200219261-00004. [PubMed: 12512212].
- Fillingim RB. Sex, gender, and pain: Women and men really are different. *Curr Rev Pain*. 2000;4(1):24–30. doi: 10.1007/s11916-000-0006-6. [PubMed: 10998712].
- 30. Unruh AM. Gender variations in clinical pain experience. *Pain*. 1996;**65**(2-3):123-67. doi: 10.1016/0304-3959(95)00214-6. [PubMed: 8826503].
- 31. Donovan KA, Taliaferro LA, Brock CW, Bazargan S. Sex differences in the adequacy of pain management among patients referred to a multidisciplinary cancer pain clinic. *J Pain Symptom Manage*. 2008;**36**(2):167–72. doi: 10.1016/j.jpainsymman.2007.09.013. [PubMed: 18395398].
- Hitt HC, McMillen RC, Thornton-Neaves T, Koch K, Cosby AG. Comorbidity of obesity and pain in a general population: Results from the Southern Pain Prevalence Study. J Pain. 2007;8(5):430–6. doi: 10.1016/ji.jpain.2006.12.003. [PubMed: 17337251].
- McCarthy LH, Bigal ME, Katz M, Derby C, Lipton RB. Chronic pain and obesity in elderly people: results from the Einstein aging study. *J Am Geriatr Soc.* 2009;57(1):115–9. doi: 10.1111/j.1532-5415.2008.02089.x. [PubMed: 19054178]. [PubMed Central: PMC2763486].
- Wright LJ, Schur E, Noonan C, Ahumada S, Buchwald D, Afari N. Chronic pain, overweight, and obesity: Findings from a community-based twin registry. *J Pain*. 2010;11(7):628–35. doi: 10.1016/j.jpain.2009.10.004. [PubMed: 20338816]. [PubMed Central: PMC2892725].
- Bigand T, Wilson M, Bindler R, Daratha K. Examining risk for persistent pain among adults with overweight status. *Pain Manag Nurs*. 2018;19(5):549-56. doi: 10.1016/j.pmn.2018.02.066. [PubMed: 29776874].
- Herishanu Y, Rogowski O, Polliack A, Marilus R. Leukocytosis in obese individuals: Possible link in patients with unexplained persistent neutrophilia. Eur J Haematol. 2006;76(6):516–20. doi: 10.1111/j.1600-0609.2006.00658.x. [PubMed: 16696775].
- Ray L, Lipton RB, Zimmerman ME, Katz MJ, Derby CA. Mechanisms of association between obesity and chronic pain in the elderly. *Pain*. 2011;152(1):53–9. doi: 10.1016/j.pain.2010.08.043. [PubMed: 20926190]. [PubMed Central: PMC3004990].
- Sandell IJ. Obesity and osteoarthritis: is leptin the link? Arthritis Rheum. 2009;60(10):2858-60. doi: 10.1002/art.24862. [PubMed: 19790076].
- Brill MJ, Diepstraten J, van Rongen A, van Kralingen S, van den Anker JN, Knibbe CA. Impact of obesity on drug metabolism and elimination in adults and children. Clin Pharmacokinet. 2012;51(5):277–304. doi:10.2165/11599410-000000000-00000. [PubMed: 22448619].
- Cheymol G. Effects of obesity on pharmacokinetics implications for drug therapy. *Clin Pharmacokinet*. 2000;39(3):215–31. doi: 10.2165/00003088-200039030-00004. [PubMed: 11020136].
- Saastamoinen P, Leino-Arjas P, Laaksonen M, Lahelma E. Socioeconomic differences in the prevalence of acute, chronic and disabling chronic pain among ageing employees. *Pain*. 2005;114(3):364– 71. doi: 10.1016/j.pain.2004.12.033. [PubMed: 15777862].
- 42. Larsson C, Hansson EE, Sundquist K, Jakobsson U. Chronic pain in older adults: Prevalence, incidence, and risk factors. *Scand J Rheumatol*. 2017;**46**(4):317–25. doi: 10.1080/03009742.2016.1218543. [PubMed: 27885914].